

CLAIMS:

1. An antibody to the human IL-12 p75 heterodimer which consists of a p₃₅ subunit and a p₄₀ subunit wherein said antibody

5 (a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

(b) is produced from a mouse which is deficient in the gene encoding said p35 subunit or the p40 subunit of IL-12.

10 2. The antibody of claim 1, wherein the antibody is a monoclonal antibody.

3. The antibody of claim 1, wherein the antibody is produced from a cell line of the mouse.

4. The antibody of claim 1, wherein the antibody cross reacts with rhesus monkey IL-12.

5. The antibody of claim 1, wherein the antibody is humanized.

6. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC 20 designation number HB-12446.

7. The antibody of claim 6, wherein the antibody is humanized.

8. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447.

9. The antibody of claim 8, wherein the antibody is humanized.

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10. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12448.

11. The antibody of claim 10, wherein the antibody is humanized.

12. The antibody of claim 1, wherein the antibody produced by a hybridoma having ATCC designation number HB-12449.

13. The antibody of claim 12, wherein the antibody is humanized.

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14. A monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said monoclonal antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

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(b) neutralizes at least about 90% of the bioactivity of human IL-12.

15. The antibody of claim 14, wherein the antibody neutralizes at least about 90% bioactivity of human IL-12 by inhibiting IL-12 stimulated PHA-activated human lymphoblast proliferation wherein

the concentration of said antibody is 0.5 μ g/ml and the concentration of said human IL-12 is 0.25 ng/ml.

16. The antibody of claim 14, wherein the antibody neutralizes at least about 90% bioactivity of 5 human IL-12 by inhibiting IL-12 stimulated IFN- γ production wherein the concentration of the antibody is 0.5 μ g/ml and the concentration of said human IL-12 is 0.25 ng/ml.

Sub D' 17. The antibody of claim 14, wherein the antibody cross reacts with rhesus monkey IL-12.

18. The antibody of claim 14, wherein the antibody is humanized.

19. The antibody of claim 14, wherein the antibody is produced by a hybridoma.

Sub C' 20. The antibody of claim 19, wherein the antibody is humanized.

21. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12446.

22. The antibody of claim 21, wherein the antibody is humanized.

23. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447.

24. The antibody of claim 23, wherein the antibody is humanized.

25. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12448.

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26. The antibody of claim 25, wherein the antibody is humanized.

27. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12449.

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28. The antibody of claim 27, wherein the antibody is humanized.

29. A hybridoma that is capable of producing a monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said antibody

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(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

b) is produced from a cell line obtained from a mouse deficient in a gene encoding said p35 subunit or said p40 subunit.

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30. The hybridoma of claim 29 wherein the hybridoma is HIL-12F3-5F2 having ATCC designation number HB-12446.

31. The hybridoma of claim 29 wherein the hybridoma is HIL-12F3-16F2 having ATCC designation number HB-12447.

32. The hybridoma of claim 29, wherein the hybridoma is HIL-12F3-20E11 having ATCC 5 designation number HB-12448.

33. The hybridoma of claim 29, wherein the hybridoma is HIL-12F3-16G2 having ATCC designation number HB-12449.

34. A method for producing an antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit, comprising the steps of:

(a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;

(b) obtaining antibodies from the immunized mammal;

(c) screening said antibodies for their ability to selectively bind an epitope presented by the p75 heterodimer to obtain said selectively binding antibody.

35. A method for producing a monoclonal antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit, comprising the 20 steps of:

(a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;

(b) harvesting antibody producing cells from the immunized mammal;

(c) forming a monoclonal antibody producing hybridoma from said cells and obtaining said monoclonal antibody;

(d) screening said monoclonal antibody produced by said hybridoma for the ability to selectively bind to an epitope presented by the p75 heterodimer to obtain said selectively binding

5 monoclonal antibody.

36. The method of claim 35, wherein the antibodies produced from the hybridoma are further screened and selected for their ability to cross react with rhesus monkey IL-12.

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